HUMAN MONOCLONAL ANTIBODIES TO SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2)

REFERNCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application Nos. 63/000,299, filed Mar. 26, 2020, 63/002,896, filed Mar. 31, 2020, 63/003,716, filed Apr. 1, 2020, 63/023,545, filed May 12, 2020, 63/024,204, filed May 13, 2020, 63/024,248, filed May 13, 2020, 63/027,173, filed May 19, 2020, 63/037,984, filed Jun. 11, 2020, 63/040,224, filed Jun. 17, 2020, 63/040,246, filed Jun. 17, 2020, 63/142,196, filed Jan. 27, 2021, and 63/161,890, filed Mar. 16, 2021, each of which is herein incorporated by reference in its entirety.

FEDERAL FUNDING DISCLOSURE

[0002] This invention was made with government support under HR0011-18-2-0001 awarded by the Defense Advanced Research Projects Agency (DARPA) and HHS Contract 75N93019C00074 awarded by the National Institutes of Allergy and Infection Disease/National Institutes of Health. The government has certain rights in the invention.

REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[0003] The content of the electronically submitted sequence listing (Name: 4815-001000C_SL_ST25.txt; Size: 87,769 Bytes; and Date of Creation: Mar. 24, 2021) is herein incorporated by reference in its entirety.

BACKGROUND

1. Field of the Disclosure

[0004] The present disclosure relates generally to the fields of medicine, infectious disease, and immunology. More particular, the disclosure relates to human antibodies binding to a novel coronavirus designated SARS-CoV-2 and methods of use therefor.

2. Background

[0005] An epidemic of a novel coronavirus (SARS-CoV-2) affected mainland China, along with cases in 179 other countries and territories. It was identified in Wuhan, the capital of China's Hubei province, after 41 people developed pneumonia without a clear cause. The virus, which causes acute respiratory disease designated coronavirus disease 2019 (COVID-19), is capable of spreading from person to person. The incubation period (time from exposure to onset of symptoms) ranges from 0 to 24 days, with a mean of 3-5 days, but it may be contagious during this period and after recovery. Symptoms include fever, coughing and breathing difficulties. An estimate of the death rate in February 2020 was 2% of confirmed cases, higher among those who require admission to hospital.

[0006] As of 10 Feb. 2020, 40,627 cases have been confirmed (6,495 serious), including in every province-level division of China. A larger number of people may have been infected, but not detected (especially mild cases). As of 10 Feb. 2020, 910 deaths have been attributed to the virus since the first confirmed death on 9 January, with 3,323 recoveries. The first local transmission outside China occurred in Vietnam between family members, while the first international transmission not involving family occurred in Germany on 22 January. The first death outside China was in the Philippines, where a man from Wuhan died on 1 February. As of 10 Feb. 2020, the death toll from this virus had surpassed the global SARS outbreak in 2003.

[0007] As of early February 2020, there is no licensed vaccine and no specific treatment, although several vaccine approaches and antivirals are being investigated. The outbreak has been declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO), based on the possible effects the virus could have if it spreads to countries with weaker healthcare systems. Thus, there is an urgent need to explore the biology and pathology of SARS-CoV-2 and well as the human immune response to this virus.

SUMMARY

[0008] Thus, in accordance with the present disclosure, there is provided a method of detecting COVID-19 infection with SARS-CoV-2 in a subject comprising (a) contacting a sample from said subject with an antibody or antibody fragment having clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively; and (b) detecting SARS-CoV-2 in said sample by binding of said antibody or antibody fragment to a SARS-CoV-2 antigen in said sample. The sample may be a body fluid, such as blood, sputum, tears, saliva, mucous or serum, semen, cervical or vaginal secretions, amniotic fluid, placental tissues, urine, exudate, transudate, tissue scrapings or feces. Detection may comprise ELISA, RIA, lateral flow assay or western blot. The method may further comprise performing steps (a) and (b) a second time and determining a change in SARS-CoV-2 antigen levels as compared to the first assay. The antibody or antibody fragment may be encoded by clone-paired variable sequences as set forth in Table1. The antibody or antibody fragment may be encoded by light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired variable sequences as set forth in Table 1, or by light and heavy chain variable sequences having 100% identity to clone-paired sequences as set forth in Table 1. The antibody or antibody fragment may comprise light and heavy chain variable sequences according to clone-paired sequences from Table 2, or light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired sequences from Table 2. The antibody or antibody fragment may bind to a SARS-CoV-2 surface spike protein. The antibody fragment may be a recombinant scFv (single chain fragment variable) antibody, Fab fragment, $F(ab')_2$ fragment, or Fv fragment.

[0009] In another embodiment, there is provided a method of treating a subject infected with SARS-CoV-2 or reducing the likelihood of infection of a subject at risk of contracting SARS-CoV-2, comprising delivering to said subject an antibody or antibody fragment having clone-paired heavy and light chain CDR sequences from Tables 3 and 4, respectively. The antibody or antibody fragment may be encoded by light and heavy chain variable sequences having at least 70%, 80%, 90% or 95% identity to clone-paired variable sequences as set forth in Table 1, or by light and heavy chain variable sequences having 100% identity to clone-paired sequences as set forth in Table 1. The antibody or antibody fragment may comprise light and heavy chain variable sequences according to clone-paired sequences